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(Srinivasula, SM., Ahmad, M., Lin, JH., Poyet, JL., Fernandes, Alnemri, T., Tsichlis, PN., Alnemri, ES, J. Biol. Chem. 18., 274(25):17946-54, (1999)).—

*R 28/04*  
Please amend the paragraph beginning on page <sup>6</sup> 4, line 34 and continuing onto page <sup>7</sup> 5 with the following amended paragraph:

-- The transcription factor NF- $\kappa$ B is sequestered in an inactive form in the cytoplasm as a complex with its inhibitor, I $\kappa$ B, the most prominent member of this class being I $\kappa$ B<sub>a</sub> (Inhibitor of nuclear factor KappaB Alpha). A number of factors are known to serve the role of stimulators of NF- $\kappa$ B activity, such as, for example, TNF. After TNF exposure, the inhibitor is phosphorylated and proteolytically removed, releasing NF- $\kappa$ B into the nucleus and allowing its transcriptional activity. Numerous genes are upregulated by this transcription factor, among them I $\kappa$ B<sub>a</sub>. The newly synthesized I $\kappa$ B<sub>a</sub> protein inhibits NF- $\kappa$ B, effectively shutting down further transcriptional activation of its downstream effectors. However, as mentioned above, the I $\kappa$ B<sub>a</sub> protein may only inhibit NF- $\kappa$ B in the absence of I $\kappa$ B<sub>a</sub> stimuli, such as TNF stimulation, for example. Other agents that are known to stimulate NF- $\kappa$ B release, and thus NF- $\kappa$ B activity, are bacterial lipopolysaccharide, extracellular polypeptides, chemical agents, such as phorbol esters, which stimulate intracellular phosphokinases, inflammatory cytokines, IL-1, oxidative and fluid mechanical stresses, and Ionizing Radiation (Basu, S., Rosenzweig, K., R., Youmell, M., Price, B., D., Biochem, Biophys, Res, Commun., 247(1):79-83, (1998)). Therefore, as a general rule, the stronger the insulting stimulus, the stronger the resulting NF- $\kappa$ B activation, and the higher the level of I $\kappa$ B<sub>a</sub> transcription. As a consequence, measuring the level of I $\kappa$ B<sub>a</sub> RNA can be used as a marker for antiapoptotic events, and indirectly, for the onset and strength of pro-apoptotic events.--